

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
14 September 2000 (14.09.2000)

PCT

(10) International Publication Number  
**WO 00/53774 A3**

(51) International Patent Classification<sup>7</sup>: **C12N 15/57**,  
15/63, 9/64, A61K 38/48, C07K 16/40, C12Q 1/37

(21) International Application Number: **PCT/US00/06237**

(22) International Filing Date: **8 March 2000 (08.03.2000)**

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:  
09/264,585 **8 March 1999 (08.03.1999) US**

(71) Applicant (for all designated States except US): **NEUROCRINE BIOSCIENCES, INC.** [US/US]; 10555 Science Center Drive, San Diego, CA 92121 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **KELNER, Gregory, S.** [US/US]; 725 Muirlands Vista Way, La Jolla, CA 92037 (US). **CLARK, Melody** [US/US]; 7075 Charmant Drive #20, San Diego, CA 92122 (US). **MAKI, Richard, A.** [US/US]; 4175-174 Porte de Palmas, San Diego, CA 92122 (US).

(74) Agents: **CHRISTIANSEN, William, T. et al.**; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW). Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM). European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

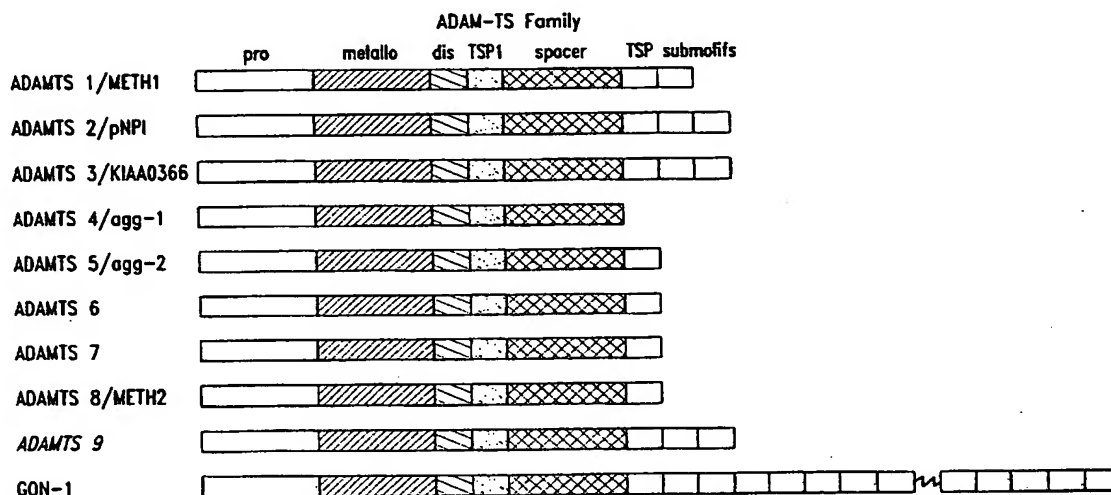
Published:

— With international search report.

(88) Date of publication of the international search report:  
**18 January 2001**

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **METALLOPROTEINASES AND METHODS OF USE THEREFOR**



(57) Abstract: Members of the ADAMTS family of metalloproteinases are provided, along with variants thereof and agents that modulate an activity of such metalloproteinases. The polypeptides and modulating agents may be used, for example, in the prevention and treatment of a variety of conditions associated with undesirable levels of metalloproteinase activity.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/06237

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/57 C12N15/63 C12N9/64 A61K38/48 C07K16/40  
C12Q1/37

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 55643 A (KUREHA CHEMICAL INDUSTRY CO., LTD.) 10 December 1998 (1998-12-10)  & EP 1 004 674 A (KUREHA CHEMICAL INDUSTRY CO., LTD.) 31 May 2000 (2000-05-31)  ---  -/--	1,3-11, 17-21, 28,29, 31,32

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

29 June 2000

Date of mailing of the international search report

13.10.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

MONTERO LOPEZ B.

## INTERNATIONAL SEARCH REPORT

International Application No

P../US 00/06237

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>KOUJI KUNO ET AL.: "Molecular cloning of a gene encoding a new type of metalloproteinase-disintegrin family protein with thrombospondin motifs as an inflammation associated gene"</p> <p>JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 1, 3 January 1997 (1997-01-03), pages 556-562, XP002076038</p> <p>MD US</p> <p>cited in the application</p> <p>abstract</p> <p>page 558, left-hand column, paragraph 2</p> <p>-page 559, left-hand column, paragraph 2; figure 2</p> <p>page 559, left-hand column, paragraph 4</p> <p>page 561, right-hand column, last paragraph</p> <p>-page 562, left-hand column, paragraph 1</p>	1,3-11, 17,20, 21,28, 29,31,32
X	<p>---</p> <p>KOUJI KUNO ET AL.: "The exon/intron organization and chromosomal mapping of the mouse ADAMTS-1 gene encoding an ADAM family protein with TPS motifs"</p> <p>GENOMICS, vol. 46, no. 3, 15 December 1997 (1997-12-15), pages 466-471, XP000922766</p> <p>cited in the application</p> <p>page 466, right-hand column, paragraph 2</p> <p>page 468, left-hand column, paragraph 5</p> <p>-page 470, right-hand column, paragraph 2; figure 3</p>	1,3-11
X	<p>---</p> <p>BOR LUEN TANG ET AL.: "ADAMTS: A novel family of proteases with an ADAM protease domain and thrombospondin 1 repeats"</p> <p>FEBS LETTERS, [Online]</p> <p>vol. 445, 26 February 1999 (1999-02-26), pages 223-225, XP002141413</p> <p>AMSTERDAM NL</p> <p>Retrieved from the Internet:</p> <p>&lt;URL:http://gdbwww.gdb.org/gdb-bin/genera/genera/hgd/Gene?!action=query&amp;displayName=ADAMTS2&gt; [retrieved on 2000-06-22]</p> <p>page 223, left-hand column, paragraph 2</p> <p>-page 225, right-hand column, paragraph 2; figure 2</p>	1,3-11
X	<p>---</p> <p>EMBL Database Entry AI378857</p> <p>Accession number AI378857; 28 January 1999</p> <p>ROBERT STRAUSBERG:"tc67h11.x1</p> <p>Soares_NhMPPu_S1 Homo sapiens cDNA clone"</p> <p>XP002141415</p> <p>the whole document</p> <p>---</p> <p>-/--</p>	1,5-7

## INTERNATIONAL SEARCH REPORT

International Application No

P /US 00/06237

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>FRANCISCA VÁZQUEZ ET AL.: "METH-1, a human ortholog of ADAMTS-1, and METH-2 are members of a new family of proteins with angio-inhibitory activity" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 33, 13 August 1999 (1999-08-13), pages 23349-23357, XP002141414 MD US abstract page 23349, right-hand column, paragraph 2 -page 23350, left-hand column, paragraph 1 page 23351, left-hand column, paragraph 1 -page 23352, right-hand column, paragraph 2; figure 1 page 23353, left-hand column, paragraph 4 -page 23357, left-hand column, paragraph 2 -----</p>	1,3-6, 8-11

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/06237

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 22-27, 30, 33-35  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims 1-12, 17-35 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 22-27, 30, 33-35

Present claims 22-27, 30 and 33-35 relate to an agent defined by reference to a desirable characteristic or property, namely decreasing or modulating expression or activity of an ADAMTS protein. The claims cover all agents having this characteristic or property, whereas the application does not provide support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for any specific example of such agents. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the agent by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, no search has been carried out for claims 22-27, 30 and 33-35.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## 1. Claims: Partially 1-12, 17-35

Polynucleotide of SEQ ID NO:1 or 23 encoding ADAMTS-2; vector and host cell comprising the same; complementary antisense molecule; use of the polynucleotide for preparing an ADAMTS-2 polypeptide; ADAMTS-2 polypeptide of SEQ ID NO:2 or 24 and variants thereof; pharmaceutical composition and vaccine comprising the same; antibody binding to the polypeptide; use of the ADAMTS-2 polynucleotide and polypeptide in screening methods and agents modulating the activity of the ADAMTS-2 protein

## 2. Claims: 36 and partially 1-12, 17-35

Polynucleotide of SEQ ID NO:3, 15 or 17 encoding ADAMTS-4; vector and host cell comprising the same; complementary antisense molecule; use of the polynucleotide for preparing an ADAMTS-4 polypeptide; ADAMTS-4 polypeptide of SEQ ID NO:4, 16 or 18 and variants thereof; pharmaceutical composition and vaccine comprising the same; antibody binding to the polypeptide; use of the ADAMTS-4 polynucleotide and polypeptide in screening methods and agents modulating the activity of the ADAMTS-4 protein

## 3. Claims: Partially 1-12, 17-35

Polynucleotide of SEQ ID NO:9 or 25 encoding ADAMTS-3; vector and host cell comprising the same; complementary antisense molecule; use of the polynucleotide for preparing an ADAMTS-3 polypeptide; ADAMTS-3 polypeptide of SEQ ID NO:10 or 26 and variants thereof; pharmaceutical composition and vaccine comprising the same; antibody binding to the polypeptide; use of the ADAMTS-3 polynucleotide and polypeptide in screening methods and agents modulating the activity of the ADAMTS-3 protein

## 4. Claims: Partially 1-12, 17-35

Polynucleotide of SEQ ID NO:13 or 21 encoding ADAMTS-5; vector and host cell comprising the same; complementary antisense molecule; use of the polynucleotide for preparing an ADAMTS-5 polypeptide; ADAMTS-5 polypeptide of SEQ ID NO:13 or 21 and variants thereof; pharmaceutical composition and vaccine comprising the same; antibody binding to the polypeptide; use of the ADAMTS-5 polynucleotide and polypeptide in screening methods and agents modulating the activity of the ADAMTS-5 protein

## 5. Claims: Partially, 1, 3-12, 17-35

Polynucleotide encoding an ADAMTS-9 protein of SEQ ID NO:27;

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

vector and host cell comprising the same; complementary antisense molecule; use of the polynucleotide for preparing an ADAMTS-9 polypeptide; ADAMTS-9 polypeptide of SEQ ID NO:27 and variants thereof; pharmaceutical composition and vaccine comprising the same; antibody binding to the polypeptide; use of the ADAMTS-9 polynucleotide and polypeptide in screening methods and agents modulating the activity of the ADAMTS-9 protein

## 6. Claims: Partially 8, 13-35

Method of preparing an ADAMTS polypeptide by culturing a transfected cell comprising a polynucleotide encoding a polypeptide of SEQ ID NO:6 or a variant thereof; ADAMTS polypeptide of SEQ ID NO:6 and variants thereof; pharmaceutical composition and vaccine comprising the same; antibody binding to the polypeptide; use of the ADAMTS polynucleotide and polypeptide in screening methods and agents modulating the activity of the ADAMTS protein

## 7. Claims: Partially 8, 13-35

Method of preparing an ADAMTS polypeptide by culturing a transfected cell comprising a polynucleotide encoding a polypeptide of SEQ ID NO:8 or a variant thereof; ADAMTS polypeptide of SEQ ID NO:8 and variants thereof; pharmaceutical composition and vaccine comprising the same; antibody binding to the polypeptide; use of the ADAMTS polynucleotide and polypeptide in screening methods and agents modulating the activity of the ADAMTS protein

## 8. Claims: Partially 8, 13-35

Method of preparing an ADAMTS polypeptide by culturing a transfected cell comprising a polynucleotide encoding a polypeptide of SEQ ID NO:12 or 20 or variants thereof; ADAMTS polypeptide of SEQ ID NO:12 or 20 and variants thereof; pharmaceutical composition and vaccine comprising the same; antibody binding to the polypeptide; use of the ADAMTS polynucleotide and polypeptide in screening methods and agents modulating the activity of the ADAMTS protein



### Information on patent family members

F ./US 00/06237

Form PCT/ISA/210 (patent family annex) (July 1992)



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&lt;210&gt; 4

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&lt;212&gt; PRT

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&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(870)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 4

Met	Arg	Leu	Glu	Trp	Ala	Ser	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Cys
1				5				10					15	
Ala	Ser	Cys	Leu	Ala	Leu	Ala	Ala	Asp	Asn	Pro	Ala	Ala	Ala	Pro
			20					25					30	Ala
Gln	Asp	Lys	Thr	Arg	Gln	Pro	Arg	Ala	Ala	Ala	Ala	Ala	Gln	Pro
		35					40					45		
Asp	Gln	Arg	Gln	Trp	Glu	Glu	Thr	Gln	Glu	Arg	Gly	His	Leu	Gln
	50					55					60			Pro
Leu	Ala	Arg	Gln	Arg	Arg	Ser	Ser	Gly	Leu	Val	Gln	Asn	Ile	Asp
65					70					75				80
Leu	Tyr	Ser	Gly	Gly	Gly	Lys	Val	Gly	Tyr	Leu	Val	Tyr	Ala	Gly
			85						90					95
Arg	Arg	Phe	Leu	Leu	Asp	Leu	Glu	Arg	Asp	Asp	Thr	Val	Gly	Ala
			100					105					110	Ala
Gly	Gly	Ile	Val	Thr	Ala	Gly	Gly	Leu	Ser	Ala	Ser	Ser	Gly	His
		115					120						125	Arg
Gly	His	Cys	Phe	Tyr	Arg	Gly	Thr	Val	Asp	Gly	Ser	Pro	Arg	Ser
	130					135					140			Leu
Ala	Val	Phe	Asp	Leu	Cys	Gly	Gly	Leu	Asp	Gly	Phe	Phe	Ala	Val
145					150					155				Lys
His	Ala	Arg	Tyr	Thr	Leu	Arg	Pro	Leu	Leu	Arg	Gly	Ser	Trp	Ala
			165						170					175
Ser	Glu	Arg	Val	Tyr	Gly	Asp	Gly	Ser	Ser	Arg	Ile	Leu	His	Val
			180					185					190	Tyr
Thr	Arg	Glu	Gly	Phe	Ser	Phe	Glu	Ala	Leu	Pro	Pro	Arg	Thr	Ser
		195					200					205		Cys
Glu	Thr	Pro	Ala	Ser	Pro	Ser	Gly	Ala	Gln	Glu	Ser	Pro	Ser	Val
	210					215					220			His
Ser	Ser	Ser	Arg	Arg	Arg	Thr	Glu	Leu	Ala	Pro	Gln	Leu	Leu	Asp
225					230					235				240
Ser	Ala	Phe	Ser	Pro	Ala	Gly	Asn	Ala	Gly	Pro	Gln	Thr	Trp	Trp
			245						250					255
Arg	Arg	Arg	Arg	Ser	Ile	Ser	Arg	Ala	Arg	Gln	Val	Glu	Leu	Leu
			260					265					270	Leu
Val	Ala	Asp	Ser	Ser	Met	Ala	Lys	Met	Tyr	Gly	Arg	Gly	Leu	Gln
		275					280					285		His
Tyr	Leu	Leu	Thr	Leu	Ala	Ser	Ile	Ala	Asn	Arg	Leu	Tyr	Ser	His
	290					295					300			Ala
Ser	Ile	Glu	Asn	His	Ile	Arg	Leu	Ala	Val	Val	Lys	Val	Val	Val
305					310					315				Leu
Thr	Asp	Lys	Ser	Leu	Glu	Val	Ser	Lys	Asn	Ala	Ala	Thr	Thr	Leu
			325						330					Lys
Asn	Phe	Cys	Lys	Trp	Gln	His	Gln	His	Asn	Gln	Leu	Gly	Asp	Asp
			340					345					350	His
Glu	Glu	His	Tyr	Asp	Ala	Ala	Ile	Leu	Phe	Thr	Arg	Glu	Asp	Leu
		355					360					365		Cys
Gly	His	His	Ser	Cys	Asp	Thr	Leu	Gly	Met	Ala	Asp	Val	Gly	Thr
	370					375					380			Ile
Cys	Ser	Pro	Glu	Arg	Ser	Cys	Ala	Val	Ile	Glu	Asp	Asp	Gly	Leu
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 Thr Phe Gly Pro Glu Tyr Ser Val Cys Pro Gly Met Asp Val Cys Ala  
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 Lys Lys Ser Lys Gly Tyr Thr Asp Val Val Arg Ile Pro Glu Gly Ala  
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 Thr His Ile Lys Val Arg Gln Phe Lys Ala Xaa Asp Gln Thr Arg Phe  
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 Thr Ala Tyr Leu Ala Leu Lys Lys Lys Thr Gly Glu Tyr Leu Ile Asn  
 770 775 780  
 Gly Lys Tyr Met Ile Ser Thr Ser Glu Thr Ile Ile Asp Ile Asn Gly  
 785 790 795 800  
 Thr Val Met Asn Tyr Ser Gly Trp Ser His Arg Asp Asp Phe Leu His  
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 Gly Met Gly Tyr Ser Ala Thr Lys Glu Ile Leu Ile Val Gln Ile Leu  
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 Ala Thr Asp Pro Thr Lys Ala Leu Asp Val Arg Tyr Ser Phe Phe Val

835                                      840                                      845  
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 Leu Val Leu Glu Arg Pro  
 865                                      870

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 <212> DNA  
 <213> Homo sapien

<400> 5  
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&lt;210&gt; 6

&lt;211&gt; 951

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 6

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Ser Pro Thr Ser Asn Ser Leu Glu Gly Gly Thr Asp Ala Thr Ala Phe
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Trp Trp Gly Glu Trp Thr Lys Trp Thr Ala Phe Ser Arg Ser Cys Gly
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Ser Val Pro Gly Pro Gly Asn Arg Thr Cys Thr Gly Thr Ser Lys Arg
85      90      95
Tyr Gln Leu Cys Arg Val Gln Glu Cys Pro Pro Asp Gly Arg Ser Phe
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Arg Glu Glu Gln Cys Val Ser Phe Asn Ser His Val Tyr Asn Gly Arg
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Thr His Gln Trp Lys Pro Leu Tyr Pro Asp Asp Tyr Val His Ile Ser
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Ser Lys Pro Cys Asp Leu His Cys Thr Thr Val Asp Gly Gln Arg Gln
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Leu Met Val Pro Ala Arg Asp Gly Thr Ser Cys Lys Leu Thr Asp Leu
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Arg Gly Val Cys Val Ser Gly Lys Cys Glu Pro Ile Gly Cys Asp Gly

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Ala	His	Leu	Gly	Tyr	Ser	Leu	Val	Thr	His	Ile	Pro	Ala	Gly	Ala	Arg
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Asp	Ile	Gln	Ile	Val	Glu	Arg	Lys	Lys	Ser	Ala	Asp	Val	Leu	Ala	Leu
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Ala	Asp	Glu	Ala	Gly	Tyr	Tyr	Phe	Phe	Asn	Gly	Asn	Tyr	Lys	Val	Asp
			260					265					270		
Ser	Pro	Lys	Asn	Phe	Asn	Ile	Ala	Gly	Thr	Val	Val	Lys	Tyr	Arg	Arg
		275					280					285			
Pro	Met	Asp	Val	Tyr	Glu	Thr	Gly	Ile	Glu	Tyr	Ile	Val	Ala	Gln	Gly
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Pro	Thr	Asn	Gln	Gly	Leu	Asn	Val	Met	Val	Trp	Asn	Gln	Asn	Gly	Lys
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Ser	Pro	Ser	Ile	Thr	Phe	Glu	Tyr	Thr	Leu	Leu	Gln	Pro	Pro	His	Glu
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Ser	Arg	Pro	Gln	Pro	Ile	Tyr	Tyr	Gly	Phe	Ser	Glu	Ser	Ala	Glu	Ser
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Gln	Gly	Leu	Asp	Gly	Ala	Gly	Leu	Met	Gly	Phe	Ile	Pro	His	Asn	Gly
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Ser	Leu	Tyr	Gly	Gln	Ala	Ser	Ser	Glu	Arg	Leu	Gly	Leu	Asp	Asn	Arg
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Gly	Pro	Pro	Arg	Gly	Lys	Gly	Phe	Arg	Asp	Arg	Asn	Val	Thr	Gly	Thr
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Pro	Leu	Thr	Gly	Asp	Lys	Asp	Asp	Glu	Glu	Val	Asp	Thr	His	Phe	Ala
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Ser	Gln	Glu	Phe	Phe	Ser	Ala	Asn	Ala	Ile	Ser	Asp	Gln	Leu	Leu	Gly
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Ile	Phe	Ala	Gln	Gly	Ala	Pro	Arg	Ser	Ser	Leu	Ala	Glu	Ser	Phe	Phe
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Val	Asp	Tyr	Glu	Glu	Asn	Glu	Gly	Ala	Gly	Pro	Tyr	Leu	Leu	Asn	Gly
			500					505					510		
Ser	Tyr	Leu	Glu	Leu	Ser	Ser	Asp	Arg	Val	Ala	Asn	Ser	Ser	Ser	Glu
		515					520					525			
Ala	Pro	Phe	Pro	Asn	Val	Ser	Thr	Ser	Leu	Leu	Thr				

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 Gly Tyr Gln Phe Arg Val Val Arg Cys Trp Lys Met Leu Ser Pro Gly  
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 Gly Arg Val Val Pro Glu Ser Gln Cys Gln Met Glu Thr Lys Pro Leu  
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&lt;210&gt; 7

&lt;211&gt; 5774

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 7

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&lt;210&gt; 8

&lt;211&gt; 1201

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 8

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Ser Leu Trp Leu Ile Ala Ala Ala Leu Val Glu Val Arg Thr Ser Ala
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Asp Gly Gln Ala Gly Asn Glu Glu Met Val Gln Ile Asp Leu Pro Ile
      20             25             30
Lys Arg Tyr Arg Glu Tyr Glu Leu Val Thr Pro Val Ser Thr Asn Leu
      35             40             45
Glu Gly Arg Tyr Leu Ser His Thr Leu Ser Ala Ser His Lys Lys Arg
      50             55             60
Ser Ala Arg Asp Val Ser Ser Asn Pro Glu Gln Leu Phe Phe Asn Ile
      65             70             75             80
Thr Ala Phe Gly Lys Asp Phe His Leu Arg Leu Lys Pro Asn Thr Gln
      85             90             95

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Leu Val Ala Pro Gly Ala Val Val Glu Trp His Glu Thr Ser Leu Val  
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 Pro Gly Asn Ile Thr Asp Pro Ile Asn Asn His Gln Pro Gly Ser Ala  
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 Thr Tyr Arg Ile Arg Lys Thr Glu Pro Leu Gln Thr Asn Cys Ala Tyr  
 130 135 140  
 Val Gly Asp Ile Val Asp Ile Pro Gly Thr Ser Val Ala Ile Ser Asn  
 145 150 155 160  
 Cys Asp Gly Leu Ala Gly Met Ile Lys Ser Asp Asn Glu Glu Tyr Phe  
 165 170 175  
 Ile Glu Pro Leu Glu Arg Gly Lys Gln Met Glu Glu Glu Lys Gly Arg  
 180 185 190  
 Ile His Val Val Tyr Lys Arg Ser Ala Val Glu Gln Ala Pro Ile Asp  
 195 200 205  
 Met Ser Lys Asp Phe His Tyr Arg Glu Ser Asp Leu Glu Gly Leu Asp  
 210 215 220  
 Asp Leu Gly Thr Val Tyr Gly Asn Ile His Gln Gln Leu Asn Glu Thr  
 225 230 235 240  
 Met Arg Arg Arg Arg His Ala Gly Glu Asn Asp Tyr Asn Ile Glu Val  
 245 250 255  
 Leu Leu Gly Val Asp Asp Ser Val Val Arg Phe His Gly Lys Glu His  
 260 265 270  
 Val Gln Asn Tyr Leu Leu Thr Leu Met Asn Ile Val Asn Glu Ile Tyr  
 275 280 285  
 His Asp Glu Ser Leu Gly Val His Ile Asn Val Val Leu Val Arg Met  
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 Arg Ser Asp Leu Asn His Ser Glu His His Asp His Ala Ile Phe Leu  
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 Thr Arg Gln Asp Phe Gly Pro Ala Gly Met Gln Gly Tyr Ala Pro Val  
 355 360 365  
 Thr Gly Met Cys His Pro Val Arg Ser Cys Thr Leu Asn His Glu Asp  
 370 375 380  
 Gly Phe Ser Ser Ala Phe Val Val Ala His Glu Thr Gly His Val Leu  
 385 390 395 400  
 Gly Met Glu His Asp Gly Gln Gly Asn Arg Cys Gly Asp Glu Thr Ala  
 405 410 415  
 Met Gly Ser Val Met Ala Pro Leu Val Gln Ala Ala Phe His Arg Tyr  
 420 425 430  
 His Trp Ser Arg Cys Ser Gly Gln Glu Leu Lys Arg Tyr Ile His Ser  
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 Tyr Asp Cys Leu Leu Asp Asp Pro Phe Asp His Asp Trp Pro Lys Leu  
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 Pro Glu Leu Pro Gly Ile Asn Tyr Ser Met Asp Glu Gln Cys Arg Phe  
 465 470 475 480  
 Asp Phe Gly Val Gly Tyr Lys Met Cys Thr Ala Phe Arg Thr Phe Asp  
 485 490 495  
 Pro Cys Lys Gln Leu Trp Cys Ser His Pro Asp Asn Pro Tyr Phe Cys  
 500 505 510  
 Lys Thr Lys Lys Gly Pro Pro Leu Asp Gly Thr Glu Cys Ala Ala Gly  
 515 520 525  
 Lys Trp Cys Tyr Lys Gly His Cys Met Trp Lys Asn Ala Asn Gln Gln

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Lys Gln Asp Gly Asn Trp	Gly Ser Trp Thr	Lys Phe Gly Ser Cys Ser		
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Arg Thr Cys Gly Thr	Gly Val Arg Phe Arg Thr	Arg Gln Cys Asn Asn		
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Pro Met Pro Ile Asn Gly Gly Gln Asp Cys Pro Gly Val Asn Phe Glu				
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Tyr Gln Leu Cys Asn Thr Glu Glu Cys Gln Lys His Phe Glu Asp Phe				
	595	600		605
Arg Ala Gln Gln Cys Gln Gln Arg Asn Ser His Phe Glu Tyr Gln Asn				
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Thr Lys His His Trp Leu Pro Tyr Glu His Pro Asp Pro Lys Lys Arg				
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Cys His Leu Tyr Cys Gln Ser Lys Glu Thr Gly Asp Val Ala Tyr Met				
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Lys Gln Leu Val His Asp Gly Thr His Cys Ser Tyr Lys Asp Pro Tyr				
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Ser Ile Cys Val Arg Gly Glu Cys Val Lys Val Gly Cys Asp Lys Glu				
	675	680		685
Ile Gly Ser Asn Lys Val Glu Asp Lys Cys Gly Val Cys Gly Gly Asp				
	690	695		700
Asn Ser His Cys Arg Thr Val Lys Gly Thr Phe Thr Arg Thr Pro Arg				
705		710		720
Lys Leu Gly Tyr Leu Lys Met Phe Asp Ile Pro Pro Gly Ala Arg His				
	725	730		735
Val Leu Ile Gln Glu Asp Glu Ala Ser Pro His Ile Leu Ala Ile Lys				
	740	745		750
Asn Gln Ala Thr Gly His Tyr Ile Leu Asn Gly Lys Gly Glu Glu Ala				
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Lys Ser Arg Thr Phe Ile Asp Leu Gly Val Glu Trp Asp Tyr Asn Ile				
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Glu Asp Asp Ile Glu Ser Leu His Thr Asp Gly Pro Leu His Asp Pro				
785		790		800
Val Ile Val Leu Ile Ile Pro Gln Glu Asn Asp Thr Arg Ser Ser Leu				
	805	810		815
Thr Tyr Lys Tyr Ile Ile His Glu Asp Ser Val Pro Thr Ile Asn Ser				
	820	825		830
Asn Asn Val Ile Gln Glu Glu Leu Asp Thr Phe Glu Trp Ala Leu Lys				
	835	840		845
Ser Trp Ser Gln Val Ser Lys Pro Cys Gly Gly Gly Phe Gln Tyr Thr				
	850	855		860
Lys Tyr Gly Cys Arg Arg Lys Ser Asp Asn Lys Met Val His Arg Ser				
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Phe Cys Glu Ala Asn Lys Lys Pro Lys Pro Ile Arg Arg Met Cys Asn				
	885	890		895
Ile Gln Glu Cys Thr His Pro Leu Trp Val Ala Glu Glu Trp Glu His				
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Cys Thr Lys Thr Cys Gly Ser Ser Gly Tyr Gln Leu Arg Thr Val Arg				
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Cys Leu Gln Pro Leu Leu Asp Gly Thr Asn Arg Ser Val His Ser Lys				
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Tyr Cys Met Gly Asp Arg Pro Glu Ser Arg Arg Pro Cys Asn Arg Val				
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Pro Cys Pro Ala Gln Trp Lys Thr Gly Pro Trp Ser Glu Cys Ser Val				
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Thr Cys Gly Glu Gly Thr Glu Val Arg Gln Val Leu Cys Arg Ala Gly  
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 Asp His Cys Asp Gly Glu Lys Pro Glu Ser Val Arg Ala Cys Gln Leu  
 995 1000 1005  
 Pro Pro Cys Asn Asp Glu Pro Cys Leu Gly Asp Lys Ser Ile Phe Cys  
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 Gln Met Glu Val Leu Ala Arg Tyr Cys Ser Ile Pro Gly Tyr Asn Lys  
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 Leu Cys Cys Glu Ser Cys Ser Lys Arg Ser Ser Thr Leu Pro Pro Pro  
 1045 1050 1055  
 Tyr Leu Leu Glu Ala Ala Glu Thr His Asp Asp Val Ile Ser Asn Pro  
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 Ser Asp Leu Pro Arg Ser Leu Val Met Pro Thr Ser Leu Val Pro Tyr  
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 Val Gly Gly Pro Asn Ala Tyr Ala Ala Phe Arg Pro Asn Ser Lys Pro  
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 Asp Gly Ala Asn Leu Arg Gln Arg Ser Ala Gln Gln Ala Gly Ser Lys  
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 His Leu Ser Ser Ala Ser Gln Met Ala Ala Ala Ser Phe Phe Ala Ala  
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 Ser Asp Ser Ile Gly Ala Ser Ser Gln Ala Arg Thr Ser Lys Lys Asp  
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 <212> DNA  
 <213> Homo sapien

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 cagtctatgg atgaacaaga agatgaagag gaacaaaaca aaccccacat catttatagg 180  
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 aacctggctg gtgacgtagc agcattaaac agcggccttag caacagaggc attttctgct 360  
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&lt;210&gt; 10

&lt;211&gt; 958

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 10

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Val Ile Ser Leu Cys Ser Gly Met Leu Gly Thr Phe Arg Ser His Asp
          20           25           30
Gly Asp Tyr Phe Ile Glu Pro Leu Gln Ser Met Asp Glu Gln Glu Asp
          35           40           45
Glu Glu Glu Gln Asn Lys Pro His Ile Ile Tyr Arg Arg Ser Ala Pro
          50           55           60
Gln Arg Glu Pro Ser Thr Gly Arg His Ala Cys Asp Thr Ser Glu His
65           70           75           80
Lys Asn Arg His Ser Lys Asp Lys Lys Lys Thr Arg Ala Arg Lys Trp
          85           90           95
Gly Glu Arg Ile Asn Leu Ala Gly Asp Val Ala Ala Leu Asn Ser Gly
          100          105          110
Leu Ala Thr Glu Ala Phe Ser Ala Tyr Gly Asn Lys Thr Asp Asn Thr
          115          120          125
Arg Glu Lys Arg Thr His Arg Arg Thr Lys Arg Phe Leu Ser Tyr Pro
          130          135          140

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 His Gly Glu Asn Leu Gln His Tyr Ile Leu Thr Leu Met Ser Ile Asp  
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 Gly Pro Ser Ile Ser Phe Asn Ala Gln Thr Thr Leu Lys Asn Leu Cys  
 180 185 190  
 Gln Trp Gln His Ser Lys Asn Ser Pro Gly Gly Ile His His Asp Thr  
 195 200 205  
 Ala Val Leu Leu Thr Arg Gln Asp Ile Cys Arg Ala His Asp Lys Cys  
 210 215 220  
 Asp Thr Leu Gly Leu Ala Glu Leu Gly Thr Ile Cys Asp Pro Tyr Arg  
 225 230 235 240  
 Ser Cys Ser Ile Ser Glu Asp Ser Gly Leu Ser Thr Ala Phe Thr Ile  
 245 250 255  
 Ala His Glu Leu Gly His Val Phe Asn Met Pro His Asp Asp Asn Asn  
 260 265 270  
 Lys Cys Lys Glu Glu Gly Val Lys Ser Pro Gln His Val Met Ala Pro  
 275 280 285  
 Thr Leu Asn Phe Tyr Thr Asn Pro Trp Met Trp Ser Lys Cys Ser Arg  
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 Lys Tyr Ile Thr Glu Phe Leu Asp Thr Gly Tyr Gly Glu Cys Leu Leu  
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 Ile Leu Tyr Asn Val Asn Lys Gln Cys Glu Leu Ile Phe Gly Pro Gly  
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 Phe Cys Arg Val Ala Gly Asn Thr Ala Tyr Tyr Gln Leu Arg Asp Arg  
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 Lys Thr Val Ala Gly Thr Phe Asn Thr Val His Tyr Gly Tyr Asn Thr

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Ser	Phe	Ser	Gly	Glu	Thr	Asp	Asp	Asp	Asn	Tyr	Leu	Ala	Leu	Ser	Ser		
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Leu	Leu	Leu	Gln	Val	Leu	Ser	Val	Gly	Lys	Leu	Tyr	Asn	Pro	Asp	Val		
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&lt;210&gt; 11

&lt;211&gt; 4303

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 11

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&lt;210&gt; 12

&lt;211&gt; 840

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 12

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1          5          10          15
Leu Trp Gly Ala Gln Pro Cys Leu Leu Leu Pro Ile Val Pro Leu Ser
20          25          30
Trp Leu Val Trp Leu Leu Leu Leu Leu Ala Ser Leu Leu Pro Ser
35          40          45
Ala Arg Leu Ala Ser Pro Leu Pro Arg Glu Glu Glu Ile Val Phe Pro
50          55          60
Glu Lys Leu Asn Gly Ser Val Leu Pro Gly Ser Gly Thr Pro Ala Arg
65          70          75          80
Leu Leu Cys Arg Leu Gln Ala Phe Gly Glu Thr Leu Leu Leu Glu Leu
85          90          95
Glu Gln Asp Ser Gly Val Gln Val Glu Gly Leu Thr Val Gln Tyr Leu
100         105         110
Gly Gln Ala Pro Glu Leu Leu Gly Gly Ala Glu Pro Gly Thr Tyr Leu
115         120         125
Thr Gly Thr Ile Asn Gly Asp Pro Glu Ser Val Ala Ser Leu His Trp
130         135         140
Asp Gly Gly Ala Leu Leu Gly Val Leu Gln Tyr Arg Gly Ala Glu Leu
145         150         155         160
His Leu Gln Pro Leu Glu Gly Gly Thr Pro Asn Ser Ala Gly Gly Pro
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Gly Ala His Ile Leu Arg Arg Lys Ser Pro Ala Ser Gly Gln Gly Pro
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Met Cys Asn Val Lys Ala Pro Leu Gly Ser Pro Ser Pro Arg Pro Arg
195         200         205
Arg Ala Lys Arg Phe Ala Ser Leu Ser Arg Phe Val Glu Thr Leu Val
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Val Ala Asp Asp Lys Met Ala Ala Phe His Gly Ala Gly Leu Lys Arg
225         230         235         240
Tyr Leu Leu Thr Val Met Ala Ala Ala Ala Lys Ala Phe Lys His Pro
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Leu	Cys	Gly	Val	Ser	Thr	Cys	Asp	Thr	Leu	Gly	Met	Ala	Asp	Val	Gly
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Asp	Asn	Gly	Tyr	Gly	His	Cys	Leu	Leu	Asp	Lys	Pro	Glu	Ala	Pro	Leu
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His	Leu	Pro	Val	Thr	Phe	Pro	Gly	Lys	Asp	Tyr	Asp	Ala	Asp	Arg	Gln
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Pro	Ala	Gln	Ala	Cys	Met	Gly	Gly	Arg	Cys	Leu	His	Met	Asp	Gln	Leu
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Gln	Asp	Phe	Asn	Ile	Pro	Gln	Ala	Gly	Gly	Trp	Gly	Pro	Trp	Gly	Pro
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Gly	Arg	Arg	Thr	Arg	Phe	Arg	Ser	Cys	Asn	Thr	Glu	Asp	Cys	Pro	Thr
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Ala	Arg	Ala	Leu	Gly	Tyr	Tyr	Tyr	Val	Leu	Glu	Pro	Arg	Val	Val	Asp
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Gly	Thr	Pro	Cys	Ser	Pro	Asp	Ser	Ser	Ser	Val	Cys	Val	Gln	Gly	Arg
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Ser	Gly	Ser	Phe	Arg	Lys	Phe	Arg	Tyr	Gly	Tyr	Asn	Asn	Val	Val	Thr

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Val Leu Val Ala Gly Asn Pro Gln Asp Thr Arg Leu Arg Tyr Ser Phe		
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Phe Val Pro Arg Pro Thr Pro Ser Thr Pro Arg Pro Thr Pro Gln Asp		
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Trp Leu His Arg Arg Ala Gln Ile Leu Glu Ile Leu Arg Arg Arg Pro		
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&lt;210&gt; 13

&lt;211&gt; 1518

&lt;212&gt; DNA

&lt;213&gt; Rattus norvegicus

&lt;400&gt; 13

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&lt;210&gt; 14

<211> 505  
 <212> PRT  
 <213> Rattus norvegicus

<400> 14

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Ala	Glu	Pro	Asp	Ser	Phe	Ala	Ala	Val	Ser	Leu	Cys	Gly	Gly	Leu	Arg
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Leu	Gln	Arg	Arg	Gly	Ala	Pro	Val	Gly	Pro	Ser	Gly	Asp	Pro	Thr	Ser
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His	Val	Phe	Asn	Met	Pro	His	Asp	Asn	Val	Lys	Val	Cys	Glu	Glu	Val
	290				295						300				
Phe	Gly	Lys	Leu	Arg	Ala	Asn	His	Met	Met	Ser	Pro	Thr	Leu	Ile	Gln
305					310					315				320	
Ile	Asp	Arg	Ala	Asn	Pro	Trp	Ser	Ala	Cys	Ser	Ala	Ala	Ile	Ile	Thr
			325					330						335	
Asp	Phe	Leu	Asp	Ser	Gly	His	Gly	Asp	Cys	Leu	Leu	Asp	Gln	Pro	Ser
		340					345					350			
Lys	Pro	Ile	Thr	Leu	Pro	Glu	Asp	Leu	Pro	Gly	Thr	Ser	Tyr	Ser	Leu
	355					360						365			
Ser	Gln	Gln	Cys	Glu	Leu	Ala	Phe	Gly	Val	Gly	Ser	Lys	Pro	Cys	Pro
	370				375					380					
Tyr	Met	Gln	Tyr	Cys	Thr	Lys	Leu	Trp	Cys	Thr	Gly	Lys	Ala	Lys	Gly
385					390					395					400



Gln Met Val Cys Gln Thr Arg His Phe Pro Trp Ala Asp Gly Thr Ser  
 405 410 415  
 Cys Gly Glu Gly Lys Phe Cys Leu Lys Gly Ala Cys Val Glu Arg His  
 420 425 430  
 Asn Pro Asn Lys Tyr Arg Val Asp Gly Pro Trp Ala Lys Trp Glu Pro  
 435 440 445  
 Tyr Gly Pro Cys Ser Arg Thr Cys Gly Gly Gly Ala Gln Leu Ala Arg  
 450 455 460  
 Arg Gln Val Gln Ala Thr Leu Pro Leu Pro Thr Gly Gly Lys Tyr Cys  
 465 470 475 480  
 Glu Gly Val Arg Val Lys Tyr Arg Ser Cys Asn Leu Glu Pro Cys Pro  
 485 490 495  
 Ser Ser Ala Ser Gly Lys Ser Phe Arg  
 500 505

<210> 15  
 <211> 1455  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1455)  
 <223> n = A,T,C or G

<400> 15  
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 ggccatggta actgtttgct ggacctacca cgaaagcaga tcctgggccc cgaagaactc 120  
 ccaggacaga cctacgatgc caccagcag tgcaacctta cattcgggcc tgagtactcc 180  
 gtgtgtcccg gcatggatgt ctgtgtctcc ctgtgggtgtg ctgtggtacg ccagggccag 240  
 atggtctgtc tgaccaagaa gcttcctgcg gtggaaggga cgccttgtgg aaaggggaga 300  
 atctgcctgc agggcaaatg tgtggacaaa accaagaaaa aatattattc aacgtcaagc 360  
 catggcaact ggggatcttg gggatcctgg ggccagtgtt ctgctcatg tggaggagga 420  
 gtgcagtttg cctatcgtcg ctgtaataac cctgtctcca gaaacaacgg acgctactgc 480  
 acagggaaga gggccatcta ccgctcctgc agtctcatgc cctgcccacc caatggtaaa 540  
 tcatttcgtc atgaacagtg tgaggccaaa aatggctatc agtctgatgc aaaaggagtc 600  
 aaaacttttg tggaatgggt tcccaaatat gcaagtgtcc tgcccagcga tgtgtgcaag 660  
 ctgacctgca gagccaaagg gactggctac tatgtggtat tttctccaaa ggtgaccgat 720  
 ggactgaat gtaggccgta cagtaattcc gtctgcgtcc gggggaagtg tgtgagaact 780  
 ggctgtgacg gcatcattgg ctcaaagctg cagtatgaca agtgcgagat atgtggagga 840  
 gacaactcca gctgtacaaa gattgttggg acctttaata agaaaagtaa gggttcanct 900  
 gacgtggtga ggattcctga aggggcaacc cacataaaag ttcgacagtt caaagccaaa 960  
 gaccagacta gattcactgc ctatttagcc ctgaaaaaga aaaacgggtga gtaccttacc 1020  
 aatggaaagt acatgatctc cacttcagag actatcattg acatcaatgg aacagtcagt 1080  
 aactatagcg gttggagcca cagggatgac ttcttgcatt gcatgggcta ctctgccacg 1140  
 aaggaaattc taatagtgca gattcttgca acagacccca ctaaaccatt agatgtccgt 1200  
 tatagctttt ttgttcccaa gaagtccact ccaaaagtaa actctgtcac tagtcatggc 1260  
 agcaataaag tgggatcaca cacttcgcag ccgcagtggg tcacgggccc atggctcgcc 1320  
 tgctctagga cctgtgacac aggttggcac accagaacgg tgcagtgccg ggatggaaac 1380  
 cggaagttag caaaaggatg tcctctctcc caaaggcctt ctgcgtttaa gcaatgcttg 1440  
 ttgaagaaat gttag 1455

<210> 16  
 <211> 484

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(484)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 16

Asp	Ala	Ser	Lys	Pro	Trp	Ser	Lys	Cys	Thr	Ser	Ala	Thr	Ile	Thr	Glu
1				5					10					15	
Phe	Leu	Asp	Asp	Gly	His	Gly	Asn	Cys	Leu	Leu	Asp	Leu	Pro	Arg	Lys
			20					25					30		
Gln	Ile	Leu	Gly	Pro	Glu	Glu	Leu	Pro	Gly	Gln	Thr	Tyr	Asp	Ala	Thr
		35					40					45			
Gln	Gln	Cys	Asn	Leu	Thr	Phe	Gly	Pro	Glu	Tyr	Ser	Val	Cys	Pro	Gly
	50					55					60				
Met	Asp	Val	Cys	Ala	Pro	Leu	Trp	Cys	Ala	Val	Val	Arg	Gln	Gly	Gln
65					70				75					80	
Met	Val	Cys	Leu	Thr	Lys	Lys	Leu	Pro	Ala	Val	Glu	Gly	Thr	Pro	Cys
				85					90					95	
Gly	Lys	Gly	Arg	Ile	Cys	Leu	Gln	Gly	Lys	Cys	Val	Asp	Lys	Thr	Lys
			100					105					110		
Lys	Lys	Tyr	Tyr	Ser	Thr	Ser	Ser	His	Gly	Asn	Trp	Gly	Ser	Trp	Gly
		115				120						125			
Ser	Trp	Gly	Gln	Cys	Ser	Arg	Ser	Cys	Gly	Gly	Gly	Val	Gln	Phe	Ala
	130					135					140				
Tyr	Arg	Arg	Cys	Asn	Asn	Pro	Ala	Pro	Arg	Asn	Asn	Gly	Arg	Tyr	Cys
145					150					155					160
Thr	Gly	Lys	Arg	Ala	Ile	Tyr	Arg	Ser	Cys	Ser	Leu	Met	Pro	Cys	Pro
				165					170					175	
Pro	Asn	Gly	Lys	Ser	Phe	Arg	His	Glu	Gln	Cys	Glu	Ala	Lys	Asn	Gly
			180					185					190		
Tyr	Gln	Ser	Asp	Ala	Lys	Gly	Val	Lys	Thr	Phe	Val	Glu	Trp	Val	Pro
		195					200					205			
Lys	Tyr	Ala	Ser	Val	Leu	Pro	Ser	Asp	Val	Cys	Lys	Leu	Thr	Cys	Arg
	210					215					220				
Ala	Lys	Gly	Thr	Gly	Tyr	Tyr	Val	Val	Phe	Ser	Pro	Lys	Val	Thr	Asp
225					230				235					240	
Gly	Thr	Glu	Cys	Arg	Pro	Tyr	Ser	Asn	Ser	Val	Cys	Val	Arg	Gly	Lys
				245					250					255	
Cys	Val	Arg	Thr	Gly	Cys	Asp	Gly	Ile	Ile	Gly	Ser	Lys	Leu	Gln	Tyr
			260				265						270		
Asp	Lys	Cys	Gly	Val	Cys	Gly	Gly	Asp	Asn	Ser	Ser	Cys	Thr	Lys	Ile
		275					280					285			
Val	Gly	Thr	Phe	Asn	Lys	Lys	Ser	Lys	Gly	Ser	Xaa	Asp	Val	Val	Arg
	290					295					300				
Ile	Pro	Glu	Gly	Ala	Thr	His	Ile	Lys	Val	Arg	Gln	Phe	Lys	Ala	Lys
305					310					315					320
Asp	Gln	Thr	Arg	Phe	Thr	Ala	Tyr	Leu	Ala	Leu	Lys	Lys	Lys	Asn	Gly
				325					330					335	
Glu	Tyr	Leu	Ile	Asn	Gly	Lys	Tyr	Met	Ile	Ser	Thr	Ser	Glu	Thr	Ile
			340					345					350		
Ile	Asp	Ile	Asn	Gly	Thr	Val	Met	Asn	Tyr	Ser	Gly	Trp	Ser	His	Arg
		355					360						365		

```

Asp Asp Phe Leu His Gly Met Gly Tyr Ser Ala Thr Lys Glu Ile Leu
 370                      375                      380
Ile Val Gln Ile Leu Ala Thr Asp Pro Thr Lys Pro Leu Asp Val Arg
385                      390                      395                      400
Tyr Ser Phe Phe Val Pro Lys Lys Ser Thr Pro Lys Val Asn Ser Val
                      405                      410                      415
Thr Ser His Gly Ser Asn Lys Val Gly Ser His Thr Ser Gln Pro Gln
                      420                      425                      430
Trp Val Thr Gly Pro Trp Leu Ala Cys Ser Arg Thr Cys Asp Thr Gly
                      435                      440                      445
Trp His Thr Arg Thr Val Gln Cys Gln Asp Gly Asn Arg Lys Leu Ala
                      450                      455                      460
Lys Gly Cys Pro Leu Ser Gln Arg Pro Ser Ala Phe Lys Gln Cys Leu
465                      470                      475                      480
Leu Lys Lys Cys

```

&lt;210&gt; 17

&lt;211&gt; 423

&lt;212&gt; DNA

&lt;213&gt; Bos taurus

&lt;400&gt; 17

```

tttagggagg agcagtgtga ggccaaaaat ggatatcagt ctgatgcaaa aggagtcaaa      60
acgtttgtgg aatgggttcc caaatatgct ggtgtcctgc ccggagacgt gtgcaaactg      120
acctgcagag ctaagggcac tggctactac gtggtgttct ctccaaagggt gaccgatggg      180
acagagtgca ggccatacag caattccgtg tgtgtccggg ggaagtgtgt gcggacaggc      240
tgtgacagca tcattggctc gaagctgcag tatgacaaat gtggcgtctg tggaggagac      300
aactccagtt gcacaaagggt ggtcgggaacc ttcaataaaa aaagtaagggt ttacactgac      360
gtcgtgagga tccccgaagg ggcgactcac ataaaagtcc gacagttcaa agccaaagac      420
cag                                         423

```

&lt;210&gt; 18

&lt;211&gt; 141

&lt;212&gt; PRT

&lt;213&gt; Bos taurus

&lt;400&gt; 18

```

Phe Arg Glu Glu Gln Cys Glu Ala Lys Asn Gly Tyr Gln Ser Asp Ala
 1                      5                      10                      15
Lys Gly Val Lys Thr Phe Val Glu Trp Val Pro Lys Tyr Ala Gly Val
                      20                      25                      30
Leu Pro Gly Asp Val Cys Lys Leu Thr Cys Arg Ala Lys Gly Thr Gly
                      35                      40                      45
Tyr Tyr Val Val Phe Ser Pro Lys Val Thr Asp Gly Thr Glu Cys Arg
                      50                      55                      60
Pro Tyr Ser Asn Ser Val Cys Val Arg Gly Lys Cys Val Arg Thr Gly
65                      70                      75                      80
Cys Asp Ser Ile Ile Gly Ser Lys Leu Gln Tyr Asp Lys Cys Gly Val
                      85                      90                      95
Cys Gly Gly Asp Asn Ser Ser Cys Thr Lys Val Val Gly Thr Phe Asn
                      100                      105                      110
Lys Lys Ser Lys Gly Tyr Thr Asp Val Val Arg Ile Pro Glu Gly Ala
                      115                      120                      125
Thr His Ile Lys Val Arg Gln Phe Lys Ala Lys Asp Gln

```

130

135

140

&lt;210&gt; 19

&lt;211&gt; 637

&lt;212&gt; DNA

&lt;213&gt; Bos taurus

&lt;400&gt; 19

```

ggaaaccctg gccatttgga gcaactacct ggccctgaag ctccccgatg gctcctatgc      60
cctcaacggt gaatacacgc tgatcccgtc cccacagac gtggtactgc ccggggccgt      120
cagcctgcgc tacagcgggg ccaactgcagc ctcggagaca ctgtcaggac acggggccct      180
ggctgagccc ttaacgctgc aggtcctagt ggctggcaac ccgcagaacg cccgcctcag      240
atacagcttt ttcgtgccgc gaccgcgacc ggtccctccc acgccacgcc ccactcccca      300
ggactggctg cgccgcaagt cacagattct ggagatcctc cggcggcgct cctgggcccgg      360
caggaaataa cctcaccatc ccggctgccc tttctgggca ccggggcctc ggacttagct      420
gggtgaacga gagacctctg cagcggcctc accccgagac atcgtggggg aggggcttag      480
tgagccccgc ctctcctccc cgcgctaccg agcaggctgg ccttgccggg gtttcctgcc      540
ctggatggct ggtggatgga aggggctggg agattgtccc ctatctaaac tgccccctct      600
gccctgctgg tcacaggagg gagggggaag gcaggga                                637

```

&lt;210&gt; 20

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Bos taurus

&lt;400&gt; 20

```

Glu Thr Leu Ala Ile Trp Ser Asn Tyr Leu Ala Leu Lys Leu Pro Asp
 1           5           10           15
Gly Ser Tyr Ala Leu Asn Gly Glu Tyr Thr Leu Ile Pro Ser Pro Thr
          20           25           30
Asp Val Val Leu Pro Gly Ala Val Ser Leu Arg Tyr Ser Gly Ala Thr
          35           40           45
Ala Ala Ser Glu Thr Leu Ser Gly His Gly Pro Leu Ala Glu Pro Leu
          50           55           60
Thr Leu Gln Val Leu Val Ala Gly Asn Pro Gln Asn Ala Arg Leu Arg
65           70           75           80
Tyr Ser Phe Phe Val Pro Arg Pro Arg Pro Val Pro Ser Thr Pro Arg
          85           90           95
Pro Thr Pro Gln Asp Trp Leu Arg Arg Lys Ser Gln Ile Leu Glu Ile
          100          105          110
Leu Arg Arg Arg Ser Trp Ala Gly Arg Lys
          115          120

```

&lt;210&gt; 21

&lt;211&gt; 1143

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1143)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 21

```

actcactata gggctcgtgc ggccgccccg gcaggatat ttaagcatcc cagcatcctc      60

```

```

aaccatcatca acatcggtgt ggtcaagggtg ctgcttctta gagatcgtga ctccggggccc 120
aagggtcaccg gcaatgcggc cctgacgctg cgcaacttct gtgcctggca gaagaagctg 180
aacaaagtga gtgacaagca ccccgagtag tgggacactg ccacccctct caccaggcag 240
gacctgtgtg gagccaccac ctgtgacacc ctgggcatgg ctgatgtggg taccatgtgt 300
gaccccaaga gaagctgtct tgtcattgag gacgatgggc ttccatcagc ctccaccact 360
gcccacgagc tggggccacgt gttcaacatg ccccatgaca atgtgaaagt ctgtgaggag 420
gtgtttggga agctccgagc caaccacatg atgtccccga ccctcatcca gatcgaccgt 480
gccaaacctt ggtcagcctg cagtgtgtgc atcatcaccg actttctgga cagcgggcac 540
ggtgactgcc tcctggacca acccagcaag cccatcttcc tgccgagnga tctgccgggc 600
gccagctaca ccctgagcca gcartgagag ctggcttttg gcgtgggctt caagccctgt 660
ccttacatgc agtactgcac caagctgtgg tgcaccggga aggccaaggg acagatgggtg 720
tgccaaacct gccacttccc ctggggccgat ggcaccagtt gtggcgaggg caagttctgc 780
ctcaaagggg cctgcgtgga aaracacaac ctcaacaagc acaggggtgga tggttcctgg 840
gccaaatggg atccctatgg cccctgtctg cgcacatgtg gtgggggctg gcagctggcc 900
aggaggcagn tgcaccaacc ccancctctg ccaacngggg gcaagtactg cgagggagtg 960
agggtgaaat accgatcctg caacctggag ccctgccccg gctcagcctc cggaaagagc 1020
ttccgggagg agcagtgtga ggctttcaac ggctacaacc acagcaccac ccggctcact 1080
ctgcgcgtgg catgggtgcc caagtactcc ggcgtgtctc cccgtgacaa gtgtaagctc 1140
atc 1143

```

&lt;210&gt; 22

&lt;211&gt; 381

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(381)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 22

```

Thr His Tyr Arg Ala Arg Ala Ala Arg Ala Gly Ile Phe Lys His
1          5          10          15
Pro Ser Ile Leu Asn Pro Ile Asn Ile Val Val Val Lys Val Leu Leu
20          25          30
Leu Arg Asp Arg Asp Ser Gly Pro Lys Val Thr Gly Asn Ala Ala Leu
35          40          45
Thr Leu Arg Asn Phe Cys Ala Trp Gln Lys Lys Leu Asn Lys Val Ser
50          55          60
Asp Lys His Pro Glu Tyr Trp Asp Thr Ala Ile Leu Phe Thr Arg Gln
65          70          75          80
Asp Leu Cys Gly Ala Thr Thr Cys Asp Thr Leu Gly Met Ala Asp Val
85          90          95
Gly Thr Met Cys Asp Pro Lys Arg Ser Cys Ser Val Ile Glu Asp Asp
100         105         110
Gly Leu Pro Ser Ala Phe Thr Thr Ala His Glu Leu Gly His Val Phe
115         120         125
Asn Met Pro His Asp Asn Val Lys Val Cys Glu Glu Val Phe Gly Lys
130         135         140
Leu Arg Ala Asn His Met Met Ser Pro Thr Leu Ile Gln Ile Asp Arg
145         150         155         160
Ala Asn Pro Trp Ser Ala Cys Ser Ala Ala Ile Ile Thr Asp Phe Leu
165         170         175
Asp Ser Gly His Gly Asp Cys Leu Leu Asp Gln Pro Ser Lys Pro Ile
180         185         190

```

Phe Leu Pro Xaa Asp Leu Pro Gly Ala Ser Tyr Thr Leu Ser Gln Gln  
 195 200 205  
 Cys Glu Leu Ala Phe Gly Val Gly Phe Lys Pro Cys Pro Tyr Met Gln  
 210 215 220  
 Tyr Cys Thr Lys Leu Trp Cys Thr Gly Lys Ala Lys Gly Gln Met Val  
 225 230 235 240  
 Cys Gln Thr Arg His Phe Pro Trp Ala Asp Gly Thr Ser Cys Gly Glu  
 245 250 255  
 Gly Lys Phe Cys Leu Lys Gly Ala Cys Val Glu Xaa His Asn Leu Asn  
 260 265 270  
 Lys His Arg Val Asp Gly Ser Trp Ala Lys Trp Asp Pro Tyr Gly Pro  
 275 280 285  
 Cys Ser Arg Thr Cys Gly Gly Gly Val Gln Leu Ala Arg Arg Gln Xaa  
 290 295 300  
 His Gln Pro Xaa Pro Leu Pro Thr Gly Gly Lys Tyr Cys Glu Gly Val  
 305 310 315 320  
 Arg Val Lys Tyr Arg Ser Cys Asn Leu Glu Pro Cys Pro Ser Ser Ala  
 325 330 335  
 Ser Gly Lys Ser Phe Arg Glu Glu Gln Cys Glu Ala Phe Asn Gly Tyr  
 340 345 350  
 Asn His Ser Thr Asn Arg Leu Thr Leu Ala Val Ala Trp Val Pro Lys  
 355 360 365  
 Tyr Ser Gly Val Ser Pro Arg Asp Lys Cys Lys Leu Ile  
 370 375 380

&lt;210&gt; 23

&lt;211&gt; 297

&lt;212&gt; DNA

&lt;213&gt; Rattus norvegicus

&lt;400&gt; 23

tccgccttc	cgggaggaac	agtgtgaaaa	atataatgcc	tacaaccaca	cggacctgga	60
tgggaatttc	cttcagtggg	tcccaata	ctcaggagt	tcccccgag	accgatgcaa	120
actgttttgc	agagcccg	ggaggagtga	gttcaaagt	tttgaaacta	aggtgatcga	180
tggcactctg	tgcggaccg	atactctggc	catctgtgtg	cggggacagt	gcgttaaggc	240
tggctgtgac	catgtggtga	actcacctaa	gaagctggac	aagtgcggtg	tctgtgtg	297

&lt;210&gt; 24

&lt;211&gt; 98

&lt;212&gt; PRT

&lt;213&gt; Rattus norvegicus

&lt;400&gt; 24

Pro	Pro	Phe	Arg	Glu	Glu	Gln	Cys	Glu	Lys	Tyr	Asn	Ala	Tyr	Asn	His
1			5						10					15	
Thr	Asp	Leu	Asp	Gly	Asn	Phe	Leu	Gln	Trp	Val	Pro	Lys	Tyr	Ser	Gly
			20					25					30		
Val	Ser	Pro	Arg	Asp	Arg	Cys	Lys	Leu	Phe	Cys	Arg	Ala	Arg	Gly	Arg
			35				40					45			
Ser	Glu	Phe	Lys	Val	Phe	Glu	Thr	Lys	Val	Ile	Asp	Gly	Thr	Leu	Cys
			50			55				60					
Gly	Pro	Asp	Thr	Leu	Ala	Ile	Cys	Val	Arg	Gly	Gln	Cys	Val	Lys	Ala
65				70					75					80	
Gly	Cys	Asp	His	Val	Val	Asn	Ser	Pro	Lys	Lys	Leu	Asp	Lys	Cys	Gly
			85					90						95	

Ile Cys

<210> 25  
 <211> 823  
 <212> DNA  
 <213> Rattus norvegicus

<400> 25  
 cccctggatg tgggtcaaagt gcagtcggaa gtacatcacc gagttcttag acactgggta 60  
 tggagagtgc ttgttaaagt aacctcaatc caggacctat cctttgcctt cccaactgcc 120  
 cggccttctc tacaacgtga ataaacaatg tgaactgatt tttggaccag gctctcaagt 180  
 gtgcccataat atgatgcagt gcagacggct ctggtgcaat aacgtggatg gagcacacaa 240  
 aggtgcagg actcagcaca cgccctgggc agatggaacc gagtgtgagc ctggaaagca 300  
 ctgcaagttt ggattctgtg ttcccaaaga aatggagggc cctgcaattg atggatcctg 360  
 gggaggttgg agtcactttg gggcctgctc aagaacatgt ggaggaggca tcagaacagc 420  
 catcagagag tgcaacagac cagagccaaa aaatggtggg aggtactgtg tagggaggag 480  
 aatraagtgc aaatcctgca acaccgagcc ctgccgaag cacaagcgag acttccgtga 540  
 ggagcagtggt gcttactttg acggcaagca tttcaacatc aatggtctgc tgcccagtggt 600  
 acgctgggtc cctaagtaca gtggaatttt gatgaaggac cgatgcaagt tgttctgcag 660  
 agtggcagga aacacagcct actaccagct tcgagacaga gtgattgacg gaacccctg 720  
 tggccaggac acaaatgaca tctgtgtcca aggcctttgc cggcaagctg gatgtgatca 780  
 tactttaaac tcaaaggccc ggaaagataa atgtgggatt tgt 823

<210> 26  
 <211> 274  
 <212> PRT  
 <213> Rattus norvegicus

<220>  
 <221> VARIANT  
 <222> (1)...(274)  
 <223> Xaa = Any Amino Acid

<400> 26  
 Pro Trp Met Trp Ser Lys Cys Ser Arg Lys Tyr Ile Thr Glu Phe Leu  
 1 5 10 15  
 Asp Thr Gly Tyr Gly Glu Cys Leu Leu Asn Glu Pro Gln Ser Arg Thr  
 20 25 30  
 Tyr Pro Leu Pro Ser Gln Leu Pro Gly Leu Leu Tyr Asn Val Asn Lys  
 35 40 45  
 Gln Cys Glu Leu Ile Phe Gly Pro Gly Ser Gln Val Cys Pro Tyr Met  
 50 55 60  
 Met Gln Cys Arg Arg Leu Trp Cys Asn Asn Val Asp Gly Ala His Lys  
 65 70 75 80  
 Gly Cys Arg Thr Gln His Thr Pro Trp Ala Asp Gly Thr Glu Cys Glu  
 85 90 95  
 Pro Gly Lys His Cys Lys Phe Gly Phe Cys Val Pro Lys Glu Met Glu  
 100 105 110  
 Gly Pro Ala Ile Asp Gly Ser Trp Gly Ser Trp Ser His Phe Gly Ala  
 115 120 125  
 Cys Ser Arg Thr Cys Gly Gly Gly Ile Arg Thr Ala Ile Arg Glu Cys  
 130 135 140  
 Asn Arg Pro Glu Pro Lys Asn Gly Gly Arg Tyr Cys Val Gly Arg Arg  
 145 150 155 160





			260					265					270				
Thr	Asp	Asn	Thr	Arg	Glu	Lys	Arg	Thr	His	Arg	Arg	Thr	Lys	Arg	Phe		
		275					280					285					
Leu	Ser	Tyr	Pro	Arg	Phe	Val	Glu	Val	Leu	Val	Val	Ala	Asp	Asn	Arg		
	290					295					300						
Met	Val	Ser	Tyr	His	Gly	Glu	Asn	Leu	Gln	His	Tyr	Ile	Leu	Thr	Leu		
305					310					315					320		
Met	Ser	Ile	Val	Ala	Ser	Ile	Tyr	Lys	Asp	Pro	Ser	Ile	Gly	Asn	Leu		
				325					330					335			
Ile	Asn	Ile	Val	Ile	Val	Asn	Leu	Ile	Val	Ile	His	Asn	Glu	Gln	Asp		
		340						345					350				
Gly	Pro	Ser	Ile	Ser	Phe	Asn	Ala	Gln	Thr	Thr	Leu	Lys	Asn	Leu	Cys		
	355						360					365					
Gln	Trp	Gln	His	Ser	Lys	Asn	Ser	Pro	Gly	Gly	Ile	His	His	Asp	Thr		
370						375					380						
Ala	Val	Leu	Leu	Thr	Arg	Gln	Asp	Ile	Cys	Arg	Ala	His	Asp	Lys	Cys		
385					390					395					400		
Asp	Thr	Leu	Gly	Leu	Ala	Glu	Leu	Gly	Thr	Ile	Cys	Asp	Pro	Tyr	Arg		
			405					410						415			
Ser	Cys	Ser	Ile	Ser	Glu	Asp	Ser	Gly	Leu	Ser	Thr	Ala	Phe	Thr	Ile		
		420						425					430				
Ala	His	Glu	Leu	Gly	His	Val	Phe	Asn	Met	Pro	His	Asp	Asp	Asn	Asn		
	435						440					445					
Lys	Cys	Lys	Glu	Glu	Gly	Val	Lys	Ser	Pro	Gln	His	Val	Met	Ala	Pro		
450					455					460							
Thr	Leu	Asn	Phe	Tyr	Thr	Asn	Pro	Trp	Met	Trp	Ser	Lys	Cys	Ser	Arg		
465					470				475						480		
Lys	Tyr	Ile	Thr	Glu	Phe	Leu	Asp	Thr	Gly	Tyr	Gly	Glu	Cys	Leu	Leu		
			485					490						495			
Asn	Glu	Pro	Glu	Ser	Arg	Pro	Tyr	Pro	Leu	Pro	Val	Gln	Leu	Pro	Gly		
		500						505					510				
Ile	Leu	Tyr	Asn	Val	Asn	Lys	Gln	Cys	Glu	Leu	Ile	Phe	Gly	Pro	Gly		
	515						520					525					
Ser	Gln	Val	Cys	Pro	Tyr	Met	Gln	Cys	Arg	Arg	Leu	Trp	Cys	Asn			
530						535				540							
Asn	Val	Asn	Gly	Val	His	Lys	Gly	Cys	Arg	Thr	Gln	His	Thr	Pro	Trp		
545					550				555						560		
Ala	Asp	Gly	Thr	Glu	Cys	Glu	Pro	Gly	Lys	His	Cys	Lys	Tyr	Gly	Phe		
			565					570						575			
Cys	Val	Pro	Lys	Glu	Met	Asp	Val	Pro	Val	Thr	Asp	Gly	Ser	Trp	Gly		
		580						585				590					
Ser	Trp	Ser	Pro	Phe	Gly	Thr	Cys	Ser	Arg	Thr	Cys	Gly	Gly	Gly	Ile		
	595					600						605					
Lys	Thr	Ala	Ile	Arg	Glu	Cys	Asn	Arg	Pro	Glu	Pro	Lys	Asn	Gly	Gly		
610					615						620						
Lys	Tyr	Cys	Val	Gly	Arg	Arg	Met	Lys	Phe	Lys	Ser	Cys	Asn	Thr	Glu		
625					630					635					640		
Pro	Cys	Leu	Lys	Gln	Lys	Arg	Asp	Phe	Arg	Asp	Glu	Gln	Cys	Ala	His		
			645					650						655			
Phe	Asp	Gly	Lys	His	Phe	Asn	Ile	Asn	Gly	Leu	Leu	Pro	Asn	Val	Arg		
		660						665				670					
Trp	Val	Pro	Lys	Tyr	Ser	Gly	Ile	Leu	Met	Lys	Asp	Arg	Cys	Lys	Leu		
	675					680						685					
Phe	Cys	Arg	Val	Ala	Gly	Asn	Thr	Ala	Tyr	Tyr	Gln	Leu	Arg	Asp	Arg		
690						695					700						

Val Ile Asp Gly Thr Pro Cys Gly Gln Asp Thr Asn Asp Ile Cys Val  
 705 710 715 720  
 Gln Gly Leu Cys Arg Gln Ala Gly Cys Asp His Val Leu Asn Ser Lys  
 725 730 735  
 Ala Arg Arg Asp Lys Cys Gly Val Cys Gly Gly Asp Asn Ser Ser Cys  
 740 745 750  
 Lys Thr Val Ala Gly Thr Phe Asn Thr Val His Tyr Gly Tyr Asn Thr  
 755 760 765  
 Val Val Arg Ile Pro Ala Gly Ala Thr Asn Ile Asp Val Arg Gln His  
 770 775 780  
 Ser Phe Ser Gly Glu Thr Asp Asp Asp Asn Tyr Leu Ala Leu Ser Ser  
 785 790 795 800  
 Ser Lys Gly Glu Phe Leu Leu Asn Gly Asn Phe Val Val Thr Met Ala  
 805 810 815  
 Lys Arg Glu Ile Arg Ile Gly Asn Ala Val Val Glu Tyr Ser Gly Ser  
 820 825 830  
 Glu Thr Ala Val Glu Arg Ile Asn Ser Thr Asp Arg Ile Glu Gln Glu  
 835 840 845  
 Leu Leu Leu Gln Val Leu Ser Val Gly Lys Leu Tyr Asn Pro Asp Val  
 850 855 860  
 Arg Tyr Ser Phe Asn Ile Pro Ile Glu Asp Lys Pro Gln Gln Phe Tyr  
 865 870 875 880  
 Trp Asn Ser His Gly Pro Trp Gln Ala Cys Ser Lys Pro Cys Gln Gly  
 885 890 895  
 Glu Arg Lys Arg Lys Leu Val Cys Thr Arg Glu Ser Asp Gln Leu Thr  
 900 905 910  
 Val Ser Asp Gln Arg Cys Asp Arg Leu Pro Gln Pro Gly His Ile Thr  
 915 920 925  
 Glu Pro Cys Gly Thr Asp Cys Asp Leu Arg Trp His Val Ala Ser Arg  
 930 935 940  
 Ser Glu Cys Ser Ala Gln Cys Gly Leu Gly Tyr Arg Thr Leu Asp Ile  
 945 950 955 960  
 Tyr Cys Ala Lys Tyr Ser Arg Leu Asp Gly Lys Thr Glu Lys Val Asp  
 965 970 975  
 Asp Gly Phe Cys Ser Ser His Pro Lys Pro Ser Asn Arg Glu Lys Cys  
 980 985 990  
 Ser Gly Glu Cys Asn Thr Gly Gly Trp Arg Tyr Ser Ala Trp Thr Glu  
 995 1000 1005  
 Cys Lys Ser Lys Ser Cys Asp Gly Gly Thr Gln Arg Arg Arg Ala Ile  
 1010 1015 1020  
 Cys Val Asn Thr Arg Asn Asp Val Leu Asp Asp Ser Lys Cys Thr His  
 1025 1030 1035 1040  
 Gln Glu Lys Val Thr Ile Gln Arg Cys Ser Glu Phe Pro Cys Pro Gln  
 1045 1050 1055  
 Trp Lys Ser Gly Asp Trp Ser Glu Val Arg Trp Glu Gly Cys Tyr Phe  
 1060 1065 1070  
 Pro

&lt;210&gt; 28

&lt;211&gt; 951

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 28

Met Gly Asp Val Gln Arg Ala Ala Arg Ser Arg Gly Ser Leu Ser Ala

1	5	10	15
His Met Leu Leu Leu Leu Leu Ala Ser Ile Thr Met Leu Leu Cys Ala			
	20	25	30
Arg Gly Ala His Gly Arg Pro Thr Glu Glu Asp Glu Glu Leu Val Leu			
	35	40	45
Pro Ser Leu Glu Arg Ala Pro Gly His Asp Ser Thr Thr Thr Arg Leu			
	50	55	60
Arg Leu Asp Ala Phe Gly Gln Gln Leu His Leu Lys Leu Gln Pro Asp			
65	70	75	80
Ser Gly Phe Leu Ala Pro Gly Phe Thr Leu Gln Thr Val Gly Arg Ser			
	85	90	95
Pro Gly Ser Glu Ala Gln His Leu Asp Pro Thr Gly Asp Leu Ala His			
	100	105	110
Cys Phe Tyr Ser Gly Thr Val Asn Gly Asp Pro Gly Ser Ala Ala Ala			
	115	120	125
Leu Ser Leu Cys Glu Gly Val Arg Gly Ala Phe Tyr Leu Gln Gly Glu			
	130	135	140
Glu Phe Phe Ile Gln Pro Ala Pro Gly Val Ala Thr Glu Arg Leu Ala			
145	150	155	160
Pro Ala Val Pro Glu Glu Glu Ser Ser Ala Arg Pro Gln Phe His Ile			
	165	170	175
Leu Arg Arg Arg Arg Arg Gly Ser Gly Gly Ala Lys Cys Gly Val Met			
	180	185	190
Asp Asp Glu Thr Leu Pro Thr Ser Asp Ser Arg Pro Glu Ser Gln Asn			
	195	200	205
Thr Arg Asn Gln Trp Pro Val Arg Asp Pro Thr Pro Gln Asp Ala Gly			
	210	215	220
Lys Pro Ser Gly Pro Gly Ser Ile Arg Lys Lys Arg Phe Val Ser Ser			
225	230	235	240
Pro Arg Tyr Val Glu Thr Met Leu Val Ala Asp Gln Ser Met Ala Asp			
	245	250	255
Phe His Gly Ser Gly Leu Lys His Tyr Leu Leu Thr Leu Phe Ser Val			
	260	265	270
Ala Ala Arg Phe Tyr Lys His Pro Ser Ile Arg Asn Ser Ile Ser Leu			
	275	280	285
Val Val Val Lys Ile Leu Val Ile Tyr Glu Glu Gln Lys Gly Pro Glu			
	290	295	300
Val Thr Ser Asn Ala Ala Leu Thr Leu Arg Asn Phe Cys Asn Trp Gln			
305	310	315	320
Lys Gln His Asn Ser Pro Ser Asp Arg Asp Pro Glu His Tyr Asp Thr			
	325	330	335
Ala Ile Leu Phe Thr Arg Gln Asp Leu Cys Gly Ser His Thr Cys Asp			
	340	345	350
Thr Leu Gly Met Ala Asp Val Gly Thr Val Cys Asp Pro Ser Arg Ser			
	355	360	365
Cys Ser Val Ile Glu Asp Asp Gly Leu Gln Ala Ala Phe Thr Thr Ala			
	370	375	380
His Glu Leu Gly His Val Phe Asn Met Pro His Asp Asp Ala Lys His			
385	390	395	400
Cys Ala Ser Leu Asn Gly Val Thr Gly Asp Ser His Leu Met Ala Ser			
	405	410	415
Met Leu Ser Ser Leu Asp His Ser Gln Pro Trp Ser Pro Cys Ser Ala			
	420	425	430
Tyr Met Val Thr Ser Phe Leu Asp Asn Gly His Gly Glu Cys Leu Met			
	435	440	445

Asp	Lys	Pro	Gln	Asn	Pro	Ile	Lys	Leu	Pro	Ser	Asp	Leu	Pro	Gly	Thr		
450						455					460						
Leu	Tyr	Asp	Ala	Asn	Arg	Gln	Cys	Gln	Phe	Thr	Phe	Gly	Glu	Glu	Ser		
465					470					475					480		
Lys	His	Cys	Pro	Asp	Ala	Ala	Ser	Thr	Cys	Thr	Thr	Leu	Trp	Cys	Thr		
				485					490					495			
Gly	Thr	Ser	Gly	Gly	Leu	Leu	Val	Cys	Gln	Thr	Lys	His	Phe	Pro	Trp		
			500					505					510				
Ala	Asp	Gly	Thr	Ser	Cys	Gly	Glu	Gly	Lys	Trp	Cys	Val	Ser	Gly	Lys		
		515					520					525					
Cys	Val	Asn	Lys	Thr	Asp	Met	Lys	His	Phe	Ala	Thr	Pro	Val	His	Gly		
	530					535					540						
Ser	Trp	Gly	Pro	Trp	Gly	Pro	Trp	Gly	Asp	Cys	Ser	Arg	Thr	Cys	Gly		
545					550				555						560		
Gly	Gly	Val	Gln	Tyr	Thr	Met	Arg	Glu	Cys	Asp	Asn	Pro	Val	Pro	Lys		
			565					570						575			
Asn	Gly	Gly	Lys	Tyr	Cys	Glu	Gly	Lys	Arg	Val	Arg	Tyr	Arg	Ser	Cys		
			580					585					590				
Asn	Ile	Glu	Asp	Cys	Pro	Asp	Asn	Asn	Gly	Lys	Thr	Phe	Arg	Glu	Glu		
		595					600					605					
Gln	Cys	Glu	Ala	His	Asn	Glu	Phe	Ser	Lys	Ala	Ser	Phe	Gly	Asn	Glu		
	610					615					620						
Pro	Thr	Val	Glu	Trp	Thr	Pro	Lys	Tyr	Ala	Gly	Val	Ser	Pro	Lys	Asp		
625					630				635						640		
Arg	Cys	Lys	Leu	Thr	Cys	Glu	Ala	Lys	Gly	Ile	Gly	Tyr	Phe	Phe	Val		
				645					650					655			
Leu	Gln	Pro	Lys	Val	Val	Asp	Gly	Thr	Pro	Cys	Ser	Pro	Asp	Ser	Thr		
			660					665					670				
Ser	Val	Cys	Val	Gln	Gly	Gln	Cys	Val	Lys	Ala	Gly	Cys	Asp	Arg	Ile		
	675						680					685					
Ile	Asp	Ser	Lys	Lys	Lys	Phe	Asp	Lys	Cys	Gly	Val	Cys	Gly	Gly	Asn		
	690					695					700						
Gly	Ser	Thr	Cys	Lys	Lys	Met	Ser	Gly	Ile	Val	Thr	Ser	Thr	Arg	Pro		
705					710				715						720		
Gly	Tyr	His	Asp	Ile	Val	Thr	Ile	Pro	Ala	Gly	Ala	Thr	Asn	Ile	Glu		
			725						730					735			
Val	Lys	His	Arg	Asn	Gln	Arg	Gly	Ser	Arg	Asn	Asn	Gly	Ser	Phe	Leu		
			740					745					750				
Ala	Ile	Arg	Ala	Ala	Asp	Gly	Thr	Tyr	Ile	Leu	Asn	Gly	Asn	Phe	Thr		
	755						760					765					
Leu	Ser	Thr	Leu	Glu	Gln	Asp	Leu	Thr	Tyr	Lys	Gly	Thr	Val	Leu	Arg		
	770					775					780						
Tyr	Ser	Gly	Ser	Ser	Ala	Ala	Leu	Glu	Arg	Ile	Arg	Ser	Phe	Ser	Pro		
785					790				795						800		
Leu	Lys	Glu	Pro	Leu	Thr	Ile	Gln	Val	Leu	Met	Val	Gly	His	Ala	Leu		
				805					810					815			
Arg	Pro	Lys	Ile	Lys	Phe	Thr	Tyr	Phe	Met	Lys	Lys	Lys	Thr	Glu	Ser		
			820					825					830				
Phe	Asn	Ala	Ile	Pro	Thr	Phe	Ser	Glu	Trp	Val	Ile	Glu	Glu	Trp	Gly		
	835						840					845					
Glu	Cys	Ser	Lys	Thr	Cys	Gly	Ser	Gly	Trp	Gln	Arg	Arg	Val	Val	Gln		
	850					855					860						
Cys	Arg	Asp	Ile	Asn	Gly	His	Pro	Ala	Ser	Glu	Cys	Ala	Lys	Glu	Val		
865					870				875						880		
Lys	Pro	Ala	Ser	Thr	Arg	Pro	Cys	Ala	Asp	Leu	Pro	Cys	Pro	His	Trp		

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 <211> 6  
 <212> PRT  
 <213> Unknown

<220>  
 <223> Semiconserved sequence of ADAMTS protein domain  
 that binds to the extracellular matrix

<400> 32  
 Phe Arg Glu Glu Gln Cys  
 1 5

<210> 33  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Oligonucleotide derived from analysis of the  
 sequences from ADAMTS-1 (mouse) and ADAMTS-3 (rat)

<221> misc\_feature  
 <222> (1)...(18)  
 <223> n = A,T,C or G

<400> 33  
 ttymgngarg arcartgy

18

<210> 34  
 <211> 18  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Oligonucleotide derived from analysis of the  
 sequences from ADAMTS-1 (mouse) and ADAMTS-3 (rat)

<221> misc\_feature  
 <222> (1)...(18)  
 <223> n = A,T,C or G

<400> 34  
 rcanaynccr cayttrtc

18

<210> 35  
 <211> 4  
 <212> PRT  
 <213> Homos sapien

<220>  
 <223> Consensus catalytic sequence site based on ADAM  
 and snake venom metalloproteases

<221> VARIANT  
<222> (3) ... (3)  
<223> Xaa = Lysine or Arginine

<221> VARIANT  
<222> (1) ... (4)  
<223> Xaa = Any Amino Acid

<400> 35  
Arg Xaa Xaa Arg  
1

<210> 36  
<211> 7  
<212> PRT  
<213> Unknown

<220>  
<223> Conserved heparin binding segment of internal TSP1  
motif of ADAM-TS family members

<221> VARIANT  
<222> (2) ... (2)  
<223> Xaa = Serine or Glycine

<221> VARIANT  
<222> (1) ... (7)  
<223> Xaa = Any Amino Acid

<400> 36  
Trp Xaa Xaa Trp Ser Xaa Trp  
1 5

<210> 37  
<211> 6  
<212> PRT  
<213> Unknown

<220>  
<223> Conserved heparin binding segment of internal TSP1  
motif of ADAM-TS family members

<400> 37  
Cys Ser Val Thr Cys Gly  
1 5

<210> 38  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 38

caggggaaac agacgatgac aact

24

<210> 39  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Primer

<400> 39

tgcggtacc caagccacac t

21

<210> 40  
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<220>  
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<400> 40

gtgcgctggg tccctaaata c

21

<210> 41  
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<220>  
 <223> Primer

<400> 41

aaaatcacag gttggcagcg g

21

<210> 42  
 <211> 12  
 <212> PRT  
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<220>  
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<400> 42

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 1 5 10

<210> 43  
 <211> 12  
 <212> PRT  
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<220>  
 <223> Zn binding site

<400> 43  
His Glu Leu Gly His Asn Phe Gly Ala Glu His Asp  
1 5 10

<210> 44  
<211> 12  
<212> PRT  
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<220>  
<223> Zn binding site

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1 5 10

<210> 45  
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<212> PRT  
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His Glu Leu Gly His Val Phe Asn Met Pro His Asp  
1 5 10

<210> 46  
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<400> 46  
His Glu Thr Gly His Val Leu Gly Met Glu His Asp  
1 5 10

<210> 47  
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<212> PRT  
<213> Homo sapien

<400> 47  
His Glu Leu Gly His Val Phe Asn Met Leu His Asp  
1 5 10

<210> 48  
<211> 12  
<212> PRT  
<213> Homo sapien

<400> 48  
His Glu Ile Gly His Leu Leu Gly Leu Ser His Asp  
1 5 10

<210> 49  
<211> 12  
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<213> Homo sapien

<400> 49

His Glu Leu Gly His Val Phe Asn Met Pro His Asp  
1 5 10

<210> 50

<211> 12

<212> PRT

<213> C. elegans

<400> 50

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<210> 51

<211> 12

<212> PRT

<213> Unknown

<220>

<223> Consensus catalytic sequence site based on ADAM  
and snake venom metalloproteases

<221> VARIANT

<222> (1)...(12)

<223> Xaa = Any Amino Acid

<400> 51

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1 5 10

